

***REMARKS***

Reconsideration of this Application is respectfully requested. Upon entry of the foregoing amendments, claims 17 and 21-40 are pending in the application, with claims 17, 21, 33 and 38 being the independent claims. Claims 1-16 and 18-20 have been canceled without prejudice or disclaimer. Support for the subject matter of the amended claims is contained in the application as originally filed. Because the foregoing changes introduce no new matter, their entry is respectfully requested.

Based on the above Amendment and the following Remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Rejections under 35 U.S.C. § 112***

The Examiner has rejected claims 1-17 under 35 U.S.C. §112, second paragraph as being indefinite. Applicants respectfully submit that the rejection of claims 1-16 are rendered moot by the cancellation thereof. Applicant's further submit that the rejection of claim 17 is overcome by the accompanying amendment thereto.

***Rejections under 35 U.S.C. § 103******Claims 1-12***

The Examiner has rejected claims 1-12 under 35 U.S.C. § 103 as being unpatentable over either U.S. Patent No. 5,240,577 to Jorgenson et al. ("the Jorgenson patent"), or U.S. Patent No. 6,402,946 to Spraul et al. ("the Spraul patent") in view of European Patent Application No. 0495255 to Chervet ("the Chervet application"). Although claims 1-12 have been cancelled without prejudice or disclaimer, the subject matter of claims 21-32 substantially conforms to that of claims 1-12, respectively.

The Jorgenson patent, the Spraul patent, and the Chervet application, taken individually or combined, fail to disclose or suggest the claimed liquid chromatography system including a micro-switching valve unit fluidly coupled to (1) chromatographic column (via a primary input port) that is supplied by a primary pump operating at a first flow rate, (2) a post-column detector (via a primary output port), and (3) a secondary pump (via a secondary input port) operating at a second flow rate substantially less than the first flow rate so as to input of individual detection peaks more slowly to the post-column detector during a peak-parking mode, as is called for by independent claim 21.

The Jorgenson patent does not teach or suggest such features. Instead, the Jorgenson patent discloses a valve assembly 10 that operates in (1) a “run” configuration during which a second pump 40 continuously forces fresh buffer coaxially past a grounded inlet end of a CZE capillary 15 (*see* column 5, lines 64 *et seq.*; FIG. 1), and (2) an “inject” configuration during which buffer input flushes the contents of storage loop 12 past CZE capillary 15 (*see* column 6, lines 8 *et seq.*). In fact, the Jorgenson patent teaches away from the present invention. The Jorgenson patent discloses that second pump 40 is a piston pump while pump 30, which supplies column 35, is a syringe pump (*see* column 6, lines 29-31), and thus fails to teach or suggest that second pump operates at a lesser flow rate. Instead, second pump 40 continuously supplies fluid to detector 51, via CZE capillary 15, regardless of the configuration of valve assembly 10, that is, the flow rate of second pump 40 does not change with respect to the “run” and “inject” configurations.

The Spraul patent also fails to disclose such features. It is the Examiner’s position that that dilution pump 86 may be utilized to pass samples to through valve unit 38 at a flow rate slower than the chromatographic speed. However, dilution pump is connected to valve unit 38 by portion 36a of capillary line 36, as is LC unit 14 (via first capillary line 32, *see* arrow 42, FIGS. 1 and 2). Thus, the Spraul patent fails to disclose a secondary pump, which operates at a lesser flow rate, that is connected to a secondary input port. Instead, dilution pump 86 is connected to the primary input port, that is, the same port as LC unit 14. While the Spraul patent discloses a secondary injection device 48/49, the Applicants note that the Spraul patent fails to

teach or suggest that device 48/49 operates at a flow rate less than that of flow source 12. Instead, the Spraul patent teaches that device 48/49 may be used to clean the flow path or park samples in the delay line (*see* column 9, lines 33-43), transfer peaks to the MS detector 26 (*see* column 10, lines 65-66), or inject solvent into the MS detector 26 to avoid that the detector runs dry (*see* column 11, lines 5-7).

The Chervet application fails to provide for the deficiencies of the Jorgenson and Spraul patents. The Chervet application fails to disclose a valve, much less a micro-switching valve unit having a secondary pump coupled to a secondary input port.

In contrast, the liquid chromatography system of the present invention includes an analysis system having a micro-switching valve unit (*e.g.*, valve unit 140) fluidly coupled to chromatographic column (*e.g.*, column 50) via a primary input port (*e.g.*, V1), which column is supplied by a primary pump (*e.g.*, pump 40) operating at a first flow rate. The micro-switching valve unit is also fluidly coupled to a post-column detector (*e.g.*, mass spectrometer unit 200) via a primary output port (*e.g.*, V2). The micro-switching valve unit is further coupled fluidly to a secondary pump (*e.g.*, syringe pump unit 240) via a secondary input port (*e.g.* V3), which secondary pump operates at a second flow rate substantially less than the first flow rate, so as to input of individual detection peaks more slowly to the post-column detector during a peak-parking mode (*see* FIG. 2C). The analysis system of the present invention provides a simplified valve configuration that is capable of pausing gradient while moving a peak of interest through the detector at a substantially lower flow rate. *See, e.g.*, page 14, lines 25 *et seq.*

For at least these reasons, Applicants respectfully submit that the Jorgenson patent, the Spraul patent and the Chervet application not render presently claim 21 obvious. Applicant submits that claims 21-32, which depend from claim 21, are allowable over the cited art for at least the same reasons noted above.

It is noted that Applicants also respectfully traverse the Examiner's rejection based on the grounds that it would have been obvious to couple the Jorgenson's controller to a pump in order to the fully automate the operation of Jorgenson's pump. Should the Examiner maintain this

rejection, Applicants respectfully request citation of a reference in support of the Examiner's position. *See M.P.E.P.* § 2144.03.

### ***Claims 13-16***

The Examiner has rejected claims 13-16 under 35 U.S.C. § 103 as being unpatentable either over the Jorgenson patent, over the Spraul patent, or over the Spraul patent in view of the Chervet application. Although claims 13-16 have been cancelled without prejudice or disclaimer, the subject matter of claims 33-37 substantially conforms to that of claims 13-17, respectively.

The Jorgenson patent, the Spraul patent, and the Chervet application, taken individually or combined, fail to disclose or suggest the claimed analysis system including a valve unit having (1) a primary input port configured for fluid coupling with the chromatographic column, (2) a primary output port for fluid coupling with the post-column detector, and (3) a secondary input port fluidly coupled to a secondary pump controlled by a control unit to pump fluid at a second flow rate substantially less than the first flow rate of a primary pump.

As noted above, the Jorgenson and Spraul patents fail to disclose a secondary pump, which operates at a lesser flow rate, that is connected to a secondary input port of a valve unit. Again, the Chervet application fails to disclose a valve.

In contrast, the analysis system of the present invention includes a valve unit (*e.g.*, valve unit 140) having a primary port (*e.g.*, V1) configured for fluid coupling to a chromatographic column (*e.g.*, column 50), which column is supplied by a primary pump (*e.g.*, pump 40) operating at a first flow rate. The valve unit is also configured for fluid coupling to a post-column detector (*e.g.*, mass spectrometer unit 200) via a primary output port (*e.g.*, V2). The valve unit is fluidly coupled to a secondary pump (*e.g.*, syringe pump unit 240) via a secondary input port (*e.g.* V3). A control unit (*e.g.*, control unit 170) is configured to operate the secondary pump at a second flow rate substantially less than the first flow rate, so as to input individual detection peaks more slowly to the post-column detector during a peak-parking mode. The

configuration of the analysis system provides a simplified valve configuration that is capable of pausing gradient while moving a peak of interest through the detector at a substantially lower flow rate. *See, e.g.*, page 14, lines 25 *et seq.*

For at least these reasons, Applicants respectfully submit that the Jorgenson patent, the Spraul patent, and the Chervet application do not render presently amended claim 33 obvious. Applicant submits that claims 34-37, which depend from claim 33, are allowable over the cited art for at least the same reasons noted above.

### ***Claims 18-20***

The Examiner has rejected claims 18-20 under 35 U.S.C. § 103 as being unpatentable over either Davis et al. (J. Am. Soc. Mass. Spectrom. 1997, 8, 1059-1069) (“the Davis publication”), or the Spraul patent. Although claims 18-20 have been cancelled without prejudice or disclaimer, the subject matter of claims 38-40 substantially conforms to that of claims 18-20, respectively.

The Davis publication and the Spraul patent, taken individually or combined, fail to disclose or suggest the claimed method which includes the step of blocking eluent outflow from a chromatographic column during a peak-parking mode and providing a secondary fluid flow at a second flow rate through the valve unit to said post-column detector during said second, peak-parking mode, wherein the second flow rate is substantially less than said first flow rate, as is called for by independent claim 38.

While the Davis publication describes extended peak parking analysis, the Davis publication fails to teach or suggest blocking eluent flow from a chromatographic column. In fact, the Davis publication does not teach or suggest valve structure used to block outflow from a chromatographic column. Instead, the Davis publication discloses that instantaneous reduction of the column head pressure (“and hence, flowrate”) to provide “peak parking”. *See, e.g.*, abstract.

Spraul patent also fails to teach or suggest blocking eluent flow from a chromatographic column. Instead, the Spraul patent discloses a switchable valve means 38 that may direct

outflow from capillary line 36 to: (1) portion 36b and MS detector 26 (FIGS. 2, 5 and 7); (2) to delay line 82, portion 36b and MS detector 26 (FIG. 3); (3) to delay line 84 and drain line 96 (FIG. 4); (4) to delay line 82 and drain line 96 (FIG. 6); (5) to delay line 82, delay line 84, portion 36b, and MS detector 27 (FIG. 8); and (6) to drain line 96 (FIG. 9). None of the illustrated positions of switchable valve means 38 blocks outflow from LC unit 14.

In contrast, the method of the present invention includes the step of blocking eluent outflow from a chromatographic column during a peak-parking mode. For example, when micro-switching valve unit 140 is in the peak-parking mode, the valve unit diverts outflow from chromatographic column 50 away from detector 200. In particular, the valve unit directs outflow to a portion of tubing 210 that is stopped by a plug 215 (*see* FIG. 2C), thereby blocking outflow from chromatographic column during the peak-parking mode.

For at least these reasons, Applicants respectfully submit that the Davis publication and the Spraul patent do not render presently amended claim 38 obvious. Applicant submits that claims 39 and 40, which depend from claim 38, are allowable over the cited art for at least the same reasons noted above.

### ***Other Matters***

#### ***Claim 17***

Applicants note that, while claim 17 was rejected by the Examiner on the basis of 35 U.S.C. § 112, claim 17 was not rejected on the basis of prior art. Applicants respectfully submit that claim 17 has been rewritten in independent form and is now allowable.

### ***CONCLUSION***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for

any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided below.

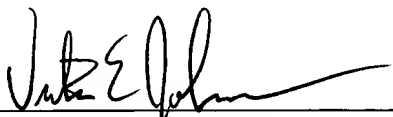
The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extension of time or additional claims, and/or credit any overpayment to Deposit Account No. 50-2319 (Order No. 465377-01023; Docket No. A-70881/DJB/VEJ).

Prompt and favorable consideration of this Amendment and Response is respectfully requested.

Respectfully submitted,

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